IN THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 12, 14, and 18 are amended, and new claims 28-32 are added.

1–11. (Cancelled).

12. (Currently amended) A method for predicting alternative splicing transcripts in tissue samples ~~using DNA chip expression data, the method~~ comprising, for each tissue sample:

~~performing test sample preparation and hybridization for a set of tissue samples during which hybridization reactions of the set of tissue samples are scanned;~~

preparing a test sample comprising labeled nucleic acid molecules having sequences that provide a match to mRNA sequences in the tissue sample;

incubating the labeled nucleic acid molecules of each test sample with an array of oligonucleotide probes having sequences of alternative splicing regions of mRNAs expressed in the tissue sample, under conditions in which hybridization of complementary nucleic acids occurs;

scanning to quantitatively detect labeled nucleic acid molecules that hybridize to the array of oligonucleotide probes;

preprocessing data resulting from the scanned hybridization reactions; and

performing a first splice variant prediction to produce first splice variant prediction data.

13. (Original) The method of claim 12, further comprising performing a second splice variant prediction to produce second splice-variant prediction data.

14. (Currently amended) The method of claim 12, wherein the steps of sample preparation, ~~and~~ hybridization, and scanning, comprises:

extracting total RNA from the set of tissue samples;

preparing double-stranded cDNA from the extracted total RNA;

performing a transcription reaction using the cDNA to produce cRNA;

purifying and quantifying the cRNA;

randomly fragmenting the cRNA;

hybridizing the randomly fragmented cRNA; and

scanning the results of hybridization.

15. (Original) The method of claim 12, wherein preprocessing data resulting from the scanned hybridization reaction comprises:

extracting raw signal intensity readings of each probe on the DNA chip in the data resulting from the scanned hybridization reaction;

normalizing the extracted raw signal intensity readings by removing noise resulting from background hybridization from the extracted raw signal intensity readings;

performing global scaling on the normalized raw signal intensity readings;

generating a normalized difference table by subtracting each mismatch signal from its corresponding perfect match signal within the normalized and scaled intensity readings; and

generating a normalized ratio table by dividing the perfect match and mismatch signals of each probe pair within the normalized and scaled intensity readings.

16. (Previously presented) The method of claim 12, wherein performing a first splice variant prediction to produce first splice variant prediction data comprises:

combining a normalized difference table and a normalized ratio table produced by the preprocessing step to generate a signal strength table;

filtering out data in the signal strength table that corresponds to uninformative probes using at least one cut-off threshold;

calculating the average difference of each probe set in each tissue sample;

calculating the average difference of each probe across different tissue samples;

calculating tissue-specific relative signal strength data by normalizing the expression level across tissues in the normalized and thresholded signal strength data; and

converting the tissue-specific relative signal strength data to a final ratio.

17. (Original) The method of claim 13, wherein performing a second splice variant prediction to produce second splice-variant prediction data comprises sorting splice variant prediction data generated by performing a first splice variant prediction to prioritize the data.

18. (Currently amended) A computer readable medium having instructions stored thereon which, when executed, cause a computer to perform one or more ~~tasks~~ steps of the method of claim 12; wherein one of the steps the computer is caused to perform is the step of performing a first splice variant prediction to produce first splice variant prediction data.

19. (Previously presented) A method for predicting alternative splicing transcripts using expression profiling data gathered using a number of different probes, comprising:

preprocessing and filtering the expression profiling data to produce normalized difference and ratio tables based on the difference of probe perfect matches and mismatches and the ratio of probe perfect matches to mismatches, respectively;

combining the difference and ratio tables to generate a signal strength table;

creating a relative signal strength table by normalizing the signal strength table across tissues represented in the expression profiling data;

calculating final ratios indicative of the differential relative expression of the probes in the tissues represented in the expression profiling data using the relative signal strength table;

selecting probes with final ratios higher than a defined threshold; and

predicting selected probes as likely alternative splicing transcripts based on one or more factors selected from the group consisting of location on a gene and proximity to other selected probes.

20. (Previously presented) The method of claim 19, wherein the final ratio is a logarithmic ratio.

21. (Previously presented) The method of claim 19, wherein combining the difference and ratio tables to create a signal strength table comprises:

creating the signal strength table using the entries in the difference table; and

assigning a default difference value for each probe pair with a ratio in the ratio table of less than a minimum ratio threshold.

22. (Previously presented) The method of claim 21, further comprising filtering the signal strength table to remove uninformative probes.

23. (Previously presented) The method of claim 22, wherein said filtering comprises replacing entries in the signal strength table that are above or below defined cut-off values with the cut-off values.

24. (Previously presented) The method of claim 23, wherein creating the relative signal strength table by normalizing the signal strength table comprises:

calculating the average difference of each probe set represented in the signal strength table in each tissue; and

for each probe set represented in the signal strength table, dividing by the average difference.

25. (Previously presented) The method of claim 19, wherein the final ratio is a logarithmic ratio of the relative signal strength of a set of probes in a particular tissue to the average relative strength of the set of probes in all tissues except the particular tissue.

26. (Previously presented) The method of claim 19, further comprising outputting a list of the selected probes identified as likely alternative splicing transcripts.

27. (Previously presented) A computer-readable medium having instructions stored thereon which, when executed, cause a computer to perform the method of claim 19.

28. (New) A computer readable medium having instructions stored thereon which, when executed, cause a computer to perform the steps of :

preprocessing data resulting from a scanned hybridization reaction obtained in a method for predicting alternative splicing transcripts in tissue samples; and

performing a first splice variant prediction to produce first splice variant prediction data.

29. (New) The computer readable medium of claim 28, wherein the step of preprocessing data resulting from a scanned hybridization reaction comprises:

extracting raw signal intensity readings of each probe on the DNA chip in the data resulting from the scanned hybridization reaction;

normalizing the extracted raw signal intensity readings by removing noise resulting from background hybridization from the extracted raw signal intensity readings;

performing global scaling on the normalized raw signal intensity readings;

generating a normalized difference table by subtracting each mismatch signal from its corresponding perfect match signal within the normalized and scaled intensity readings; and

generating a normalized ratio table by dividing the perfect match and mismatch signals of each probe pair within the normalized and scaled intensity readings.

30. (New) The computer readable medium of claim 28, wherein the step of performing a first splice variant prediction to produce first splice variant prediction data comprises:

combining a normalized difference table and a normalized ratio table produced by the preprocessing step to generate a signal strength table;

filtering out data in the signal strength table that corresponds to uninformative probes using at least one cut-off threshold;

calculating the average difference of each probe set in each tissue sample;

calculating the average difference of each probe across different tissue samples;

calculating tissue-specific relative signal strength data by normalizing the expression level across tissues in the normalized and thresholded signal strength data; and

converting the tissue-specific relative signal strength data to a final ratio.

31. (New) The computer readable medium of claim 28, which also has instructions stored thereon which, when executed, cause a computer to perform a second splice variant prediction to produce second splice-variant prediction data.

32. (New) The computer readable medium of claim 31, wherein performing a second splice variant prediction to produce second splice-variant prediction data comprises sorting splice variant prediction data generated by performing a first splice variant prediction to prioritize the data.